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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/529,659	06/22/2000	ERNST WAGNER	0652.2050000	1008

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STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W., SUITE 600
WASHINGTON, DC 20005-3934

EXAMINER
YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
1642	16

DATE MAILED: 01/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/529,659	WAGNER ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The examiner of the application has changed. This case has now been transferred as of 1/21/2003. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Christopher Yaen, Group Art Unit 1642.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 111/2002 has been entered.

3. The amendment filed 11/1/2002 (paper no 15) is acknowledged. Accordingly, claims 15, 20,22,23, and 26-28 are amended. Claims 29-38 are newly added. Therefore, claims 15-38 are pending and examined on the record.

Claim Rejections Withdrawn - 35 USC § 112, 2nd paragraph

4. The rejection of claims 15-28 under 35 USC 112, 2nd paragraph as being indefinite, is withdrawn in view of the arguments and amendments set forth by the applicant.

Claim Rejections Withdrawn - 35 USC § 103

5. The rejection of claims 15-28 under 35 USC 103(a) as being obvious over Porgador *et al* in view of Saravolac *et al*, Cleland *et al,* or Fujioka *et al* is withdrawn in view of the persuasive arguments set forth by the applicant.

6. ***New Claim Rejections - 35 USC § 112,1st paragraph***

7. Claims 15-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a tumor treatment, does not reasonably provide enablement for a tumor vaccine. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni,

195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The nature of the invention: The claims of the instant invention are drawn to a tumor vaccine comprising a tumor antigen source and an IFNγ release system.

The state of the prior art and the predictability or lack thereof in the art: The art teaches that the preparation of tumor vaccines are often unpredictable. Furthermore, the determining which members within a given population are to actually receive the vaccine is often unpredictable because the art for predetermining which patients are to develop cancer has not been fully elucidated. One example in the art, that teaches the unpredictability of vaccines, is provided by Evans *et al* (Q. J. Med 1999;92:299-307). Evans *et al* teach that the use of tumor vaccines is far from being fully understood, and that the use of such vaccines in cancer treatment "still belongs to the realm of fiction."

The amount of direction or guidance present and the presence or absence of working examples: The examples of the instant invention have provided a medicament for the treatment of cancer. However, no wherein the specification does it teach how to administer a vaccine so as to prevent the formation of a cancer. The use of the instant invention is enabled as a curative product used to help in the reduction or elicitation of a tumor through the generation of an immune response. No where in the specification

does it teach how to prevent the formation of tumor through the administration of a prophylaxis. As such, one of skill in the art would be forced to experiment in terms of determining who would need or require the use of such a compound, who amoungst the population would develop cancer, and whether the vaccine would function as prescribed in the claims of instant invention.

The breadth of the claims and the quantity of experimentation needed: Given the unpredictability within the art of immune system regulation, the unpredictability of tumor vaccines, and absent sufficient teachings in the specification to overcome the teachings of unpredictability found in the art, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

New Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 15-17, 22, and 24-30 rejected under 35 U.S.C. 102(b) as being anticipated by Golumbek *et al* (Cancer Research 1993 Dec; 53;5841-5844, IDS AT5). Claims are drawn to a tumor vaccine comprising a tumor antigen source and a IFNγ release system, wherein the effective dosage range of IFNγ is between 50ng to 5μg, wherein the IFNγ release system comprises microspheres, wherein the tumor antigen source consists of allogenic tumor cells which comprise peptides, or an antigen presenting cell comprising a tumor antigen, and wherein the vaccine further comprises

one other cytokine contained within the IFNγ release system. Golumbek *et al* teach a tumor vaccine that comprises a tumor antigen source and an IFNγ release system, wherein the tumor antigen source is a melanoma cell that comprises tumor associated antigens, which is also an antigen presenting cell, wherein the IFNγ release system comprises a microsphere and further inherently will comprise a release of another cytokine, namely IL-12, and wherein the effective dosage ranges is within the specified weights of the 50ng to 5μg. These weights are encompassed within the concentrations disclosed by Golumbeck because the volume of the vaccine claimed is not given, therefore, as currently interpreted, the weights fall within the concentrations specified in the art.

New Claim Rejections - 35 USC § 103

10. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

11. Claims 15-20, 22-26, and 28-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Golumbek *et al* (Cancer Research 1993 Dec; 53;5841-5844, IDS AT5) in view of Porgador *et al* (J. Immunol 1993;150:1458-1470, IDS AS10). Claims are drawn to a tumor vaccine comprising a tumor antigen source and an IFNγ release system, wherein the dosage of IFNγ is between 50ng to 5 μg and has a release time of ½ an hour to 3 days, wherein the IFNγ release system is a liposome, a microsphere, or a minipellet containing IFNγ, wherein the tumor antigen source consists of tumor cells, which could be allogeneic, that comprise peptides derived from a tumor antigen. The claims are also drawn to the said tumor vaccine further comprising additional cytokines,

that are to be released from an additional cytokine release system that is a liposome, a microsphere, or a minipellet. The claims are further drawn to a tumor vaccine wherein the additional cytokine is release from a tumor cell expressing said additional cytokine.

Golumbek *et al* teach that a biodegradable release system comprising a biodegradable polymer, such as a microsphere, and a cytokine could be used in conjunction with tumor cells as a vaccine to elicit a T-cell immune response. Golumbak *et al* further suggest that a polymer release system containing a cytokine separate from that of a cell is more effective because the separate systems require less labor and yet still extremely effective in delivering sustained release of cytokine in an therapeutically effective manner (see introduction page 5841).

Porgador *et al* teach the expression and administration of a tumor cell that expresses tumor associated antigens and a cytokine introduced into the cell through transfection.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to manufacture a tumor vaccine comprising a tumor antigen source and a cytokine release system so as to elicit an immune response against a tumor antigen. One of ordinary skill would have been motivated to do so because at the time of filing, it was readily known in the art that the administration of deactivated tumor cells comprising tumor associated antigens (TAA) to patients suffering from cancers associated with the said TAA was an effective method of generating an immune response against said cancer, and that the addition of adjuvants that help in the elicitation of an immune response was also in practice. It was also

known at the time of the invention that vaccines comprising deactivated tumor cells expressing cytokines was also being used in the treatment of cancers (see Porgador *et al*) but less proficient because of the labor intensive preparation of the vaccine (see Glombak *et al*). Further, it was already known that the separation of the deactivated tumor cell and the cytokine would be more efficient and yet retain the same elicitation of immune response because Golumbak *et al* teach such separation and shows that this is a more efficient and less labor intensive method of generating the same and if not more effective elicitation of immune response. It would have also been obvious to one of skill in the art to substitute liposomes and mimipellets place of the microspheres because they have been well established forms of controlled release biopolymers. It would have also been *prima facie* obvious to use the claimed dose ranges because those could have been ascertained through routine experimentation. One of ordinary skill in the art would have expected a reasonable expectation of success because the general vaccine components, namely the tumor antigen bearing cells and a release system containing a cytokine, and its usage in eliciting an immune response was already shown to be effective in the art. And lastly, although there has not been specific art cited to obviate the specified release times, dosage of IFNγ, and biodegradable polymers of the IFNγ release system, it is considered a design choice by the applicant of which the specification has not shown criticality of the limitations to merit non-obviousness over the prior art.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
January 27, 2003

ALI R. SALIMI
PRIMARY EXAMINER